2023

Is mindfulness- based stress reduction (MBSR) more effective than standard care in reducing anxiety in breast cancer survivors with a diagnosis of Stage 0 – III breast cancer?

Emma Poulshock
Philadelphia College of Osteopathic Medicine

Is mindfulness- based stress reduction (MBSR) more effective than standard care in reducing anxiety in breast cancer survivors with a diagnosis of Stage 0 – III breast cancer?

Emma Poulshock, PA-S

A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

December 16, 2022

ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not "is mindfulness- based stress reduction (MBSR) more effective than standard care in reducing anxiety in breast cancer survivors with a diagnosis of Stage 0 – III breast cancer?"

STUDY DESIGN: Review of three randomized control trials (RCT).

DATA SOURCES: All three RCTs were published in English and taken from peer-reviewed journals using PubMed. The articles were published between 2012-2021.

OUTCOMES MEASURED: The outcome measured included reduction in anxiety using the State-Trait Anxiety Inventory and POMS total mood disturbance (and its subscale of anxiety).

RESULTS: In the 2014 RCT led by Lengacher et al, there was no significant difference between MBSR and usual care, indicated by a p-value of 0.17. The 2021 RCT study led by Lengacher et al. showed a reduction in anxiety in the MBSR group compared to the UC group, indicated by a p-value of 0.01 and a mean change from baseline of 3.8. The RCT led by Hoffman et al. showed a statistically significant difference between the MBSR and UC groups. There was a mean change adjusted at baseline of 2.93 and a 95% confidence interval of -4.67 to -1.20.

CONCLUSION: This systemic review had inconclusive results and could not determine if MBSR is more effective than standard care in reducing anxiety in breast cancer survivors.

KEY WORDS: Breast Cancer Survivors (BCS), Mindfulness-Based Stress Reduction (MBSR)

INTRODUCTION

Breast cancer comprises the largest population of cancer survivors in the United States. The increase in screening methods and treatments has led to a 5-year survival rate of 90% amongst breast cancer patients.[1] Despite improved treatment options and high survival rates, breast cancer patients continue to experience long term psychological burdens. Fear of recurrence (FOR) has been identified as a top concern for breast cancer survivors (BCS).[1,2] The uncertainty about cancer recurrence creates high levels of stress and anxiety. Fear of recurrence contributes to a decreased quality of life leading to increased depressive symptoms, anxiety, fatigue, and poor emotional and physical well-being.[1] Between 24-89% of breast cancer survivors suffer from fear of recurrence, which persists years after treatment.[3]

Studies show that survivors that experience greater FOR will require an increase in healthcare utilization.[1] While an exact estimate regarding annual health care utilization is unknown, breast cancer survivors require annual screenings, follow ups with general practitioners, complementary and alternative medicine, and supportive counseling.[4] BCS with anxiety will frequently seek out healthcare specialists, resulting in a significant number of healthcare visits each year.[4] Additionally, anxiety has been associated with refusal of discharge from cancer centers amongst survivors and fear of recurrence has been shown to persist up to 32 years after surgery.[3,4] The wide variety of needs and healthcare visits of BCS contributes to a substantial amount of costs annually. There is an association between higher health-related anxiety and more frequent visits leading to increased outpatient costs.[4] The annual cost to support breast cancer survivors with anxiety has not been identified. However, a study from 2016, showed that the annual economic burden, including the sum of medical expenditures and productivity losses was $14,167 for nonelderly and $14,391 for elderly.[5]

While many resources exist to treat anxiety amongst the general population, there are few interventions that have been tested to treat fear of recurrence.[3] Treatment for anxiety includes psychotherapy, physical activity, stress management, meditation, and medications. These standard methods of care have been utilized for BCS with anxiety, but there is limited research focused on how breast cancer survivors cope with fear of recurrence and anxiety.[2] BCS suffer from multiple co-occurring physical and psychological symptoms that can lead to a poor quality of life and therefore there is a clinical need for intervention.[3,6]

Over the last several years, research has been studying the use of mindfulness based-stress reduction for cancer survivors. Mindfulness-based stress reduction (MBSR) is a program focusing on the power of mindfulness to help patients regulate awareness and attention.[3] MBSR encompasses breath awareness, body scan, walking meditation, sitting meditation and yoga.[3] The purpose of this approach is for survivors to learn how to self-regulate their emotions during distress and to reduce anxiety for patients.[3] This paper evaluates three randomized controlled trials (RCTs), assessing the efficacy of MBSR as an intervention for anxiety of breast cancer survivors.

OBJECTIVE

The objective of this selective EBM review is to determine whether or not "is mindfulness- based stress reduction (MBSR) more effective than standard care in reducing anxiety in breast cancer survivors with a diagnosis of Stage 0 – III breast cancer?"

METHODS

The population targeted for this review included breast cancer survivors diagnosed with stage 0-III breast cancer. The demographics and characteristics of the population can be found in Table 1. The intervention used in each study was mindfulness-based stress reduction (MBSR) in

comparison to standard care. The outcome measured was reduction in anxiety for breast cancer survivors. The studies were chosen based on relevance to the clinical question and if they fulfilled the criteria of a patient-oriented outcome. All articles selected were published in English in peer-reviewed journals and obtained from PubMed. Keywords used included "breast cancer survivors" and "Mindfulness-Based Stress Reduction". Inclusion criteria consisted of randomized control trials (RCTs) published within the last 10 years. Exclusion criteria consisted of any secondary research and all studies published before 2010. Statistics reported in the studies included p-values and mean change from baseline. Hoffman et al. used confidence intervals.

OUTCOMES MEASURED

The outcome measured in this review is reduction in anxiety. The two studies by Lengacher et al measured anxiety with the State-Trait Anxiety Inventory. The STAI is a two 20-item scale measuring state anxiety (present anxiety) and trait anxiety (long term anxiety).[3] The scale range is from 20-80 with a possible score of (1) indicating "not at all" to (4) "almost always".[3] Higher scores indicate more anxiety. In the study by Hoffman et al. anxiety was measured using the Profile of Mood States (POMS) total mood disturbance with subscales that evaluate anxiety, depression, anger, vigor, fatigue, and confusion.[6] The POMS is a 65-item test with lower scores indicative of improvement in mood.[6]

RESULTS

All three studies in this review enrolled breast cancer survivors with diagnosis of Stage 0-III breast cancer and evaluated the efficacy of MBSR. Lengacher et al. conducted a randomized control trial comparing the usual care to MBSR. A total of 84 breast cancer survivors were recruited from H. Lee Moffitt Cancer Center and Research Institute based on the inclusion and exclusion criteria noted in Table 1.[3] Participants were randomly assigned in a 1:1 ratio to MBSR,

Table 1. Demographics & Characteristics of Included Studies

Study	Type	# Pts	Age (yrs.)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Lengacher[3] (2014)	RCT	84	Females ≥ 55	Women diagnosed with primary stage 0, I, II, or III breast cancer and completed treatment within the prior 18 months, able to read and speak English at 8th grade level	Stage IV breast cancer, mastectomy, severe psychiatric diagnosis, and breast cancer recurrence	2	6-week MBSR program including use of four meditative practices (sitting meditation, walking meditation, body scan and yoga). Weekly 2-hour sessions conducted by MBSR trained psychologist.
Lengacher[4] (2021)	RCT	322	Females ≥ 21	Women with a diagnosis of Stage 0-III breast cancer, lumpectomy and/or mastectomy and/or adjuvant radiation or chemotherapy	Stage IV breast cancer, severe mental disorder, and/or breast cancer recurrence	23	6-week MBSR (2-hour) sessions including training in 4 formal meditation techniques (sitting meditation, walking meditation, body scan and gentle hatha yoga).
Hoffman[5] (2012)	RCT	229	Females 18-80	Women with a diagnosis of Stage 0-III breast cancer, aware of cancer diagnosis, able to complete questionaries, within 2 months – 2 years after completion, of surgery, chemotherapy, and or radiation.	Stage IV breast cancer, men, did not speak English, could not give informed consent as a result of psychosis or intellectual impairment, or suffered from substance misuse, suicidal thoughts or current psychosis.	15	8-week MBSR divided into 2-hour classes and one 6-hour day of mindfulness in week 6. Class consisted of formal mindfulness practices: body scan, gentle and appropriate lying and standing yoga stretches, sitting meditation, group discussions, didactic teaching, and home practices.

or usual care (UC) groups and then stratified using a random number generator based on cancer stage and treatment received.[3] Of the participants enrolled, 82 completed the study with 42 patients in the UC group and 40 in the MBSR group.[3] There were 2 participants who were lost to follow up and the losses were equal across each studied group, but a worst-case analysis was not performed.[3] The participants of the MBSR group followed the 6-week program that was adapted upon Kabat-Zinn's 8-week program. The program included use of four meditative practices (sitting meditation, walking meditation, body scan and yoga), as well as attendance in weekly 2-hour sessions conducted by a trained psychologist.[3] Subjects participated in formal meditation for 15-45 minutes per day 6 days per week and informal meditation daily.[3] All subjects in the MBSR group were required to record home practices in a diary daily.

The primary outcome analyzed in this paper is mean state and trait anxiety, which was measured using the State-Trait Anxiety Inventory after the 6-week MBSR program. At baseline, there was a significant difference in the mean state anxiety between the UC and MBSR groups. Mean state anxiety was higher in the control group than MBSR.[3] The results are summarized in Table 2 below. The MBSR group's state anxiety improved by 1.4 compared to the UC group after 6 weeks. The mean change in anxiety between the MBSR and UC group was 1.4 and the p-value between the two groups was 0.17. These results suggest that there was no significant difference in anxiety between the two groups. The conclusion of the results is complicated by the fact that the mean state anxiety was higher in the control group than MBSR. It is difficult to determine if MBSR therapy would have been more effective in a group of patients that had a higher mean state anxiety at baseline. Therefore, although there was no difference statistically speaking, potential bias and validity of the results exists due to the change amongst the two groups at baseline.

Table 2. Mean Values of Potential Mediators (Anxiety) at Pre-intervention and at 6 weeks [3]

	Pre-intervention	Mean Change Anxiety (Calculated)	P-value	Change at week 6	Mean Change Anxiety (Calculated)	P-value
Usual care	40.4	5.1	0.05	6.4	1.4	0.17
MBSR	35.3			7.8		

Lengacher et al. conducted another randomized control trial published in 2021 comparing UC and MBSR. Subjects were randomly assigned in a 1:1 ratio and stratified by type of surgery, treatment, and stage of breast cancer.[7] All data collected was blinded, including lab technicians and scoring.[7] A total of 322 participants were enrolled in the study. Of the 322 participants, 23 subjects did not return for repeat assessments, leaving 299 participants who completed the study. Participants analyzed included 155 in the UC group and 167 in the MBSR group. Similarly, to Lengacher's other RCT, the MBSR group attended 6 weekly (2-h) sessions conducted by a trained psychologist and participated in at home practices that was recorded in a diary.[7] The usual care group was asked not to practice meditation or yoga but were allowed to attend standard post-treatment clinic visits.[7]

At baseline, MBSR participants presented with higher state anxiety compared to UC participants. Therefore, subgroup analyses were conducted assessing fear of recurrence as a mediator of anxiety at 6 weeks and 12 weeks.[7] Table 3 depicts the mean change of state anxiety at 6 weeks. A statistically significant difference was measured as a p-value of 0.01 between the two interventions. MBSR was found to be superior to UC reflected by the 3.8 difference. Again, statistically he results were significant. However, at baseline the MBSR group had a greater state anxiety, which could contribute to MBSR therapy being more successful than usual care. On the other hand, Lengacher's 2014 RCT suggested no significant difference and the usual care group

had higher anxiety than the MBSR group at baseline. Therefore, the results from both studies are questionable due to the varying levels of anxiety at baseline.

Table 3. Effects of MBSR on Mean Change of State Anxiety at 6 weeks[7]

	Baseline to 6-weeks	Mean Change Anxiety (Calculated)	P-value
Usual care	2.6	3.8	0.01
MBSR	6.4		

Hoffman et al. conducted a randomized control trial that compared UC and MBSR. Participants were recruited from the London Haven psychology center and received an average of 30 hours of support prior to entry.[6] Random assignment was performed using a computer generator ensuring allocation concealment.[6] The 8-week program consisted of 8 weekly (2h) length classes following formal mindfulness practices, as well as at home practice for 40-45 minutes 6-7d/week.[6] A total of 229 participants were recruited with 214 people completing the study. There were 15 participants who dropped out of the study leaving 111 analyzed in the UC group and 103 analyzed in the MBSR group.[6]

Table 4. Primary Outcome for POMS Total Mood Disturbance and Subscale of Anxiety and Estimates of mean, SD, and CI

	Mean	Mean difference between groups adjusted at baseline	SD	95% CI
Usual care	13.36	2.93	7.20	-4.67 to -1.20
MBSR	10.32		7.0	

The outcomes were measured at baseline (T1), weeks 8-12 (T2), and weeks 12-14 (T3). Table 4 summarizes the results at 8 weeks (T2), including mean, SD, and 95% confidence interval. The mean difference between groups adjusted at baseline was 2.93 suggesting that the MBSR had a greater reduction in anxiety. The 95% confidence interval was -4.67 to -1.20, which

is a narrow confidence interval. This interval illustrates that in repeat studies it is expected for participants to have a reduction in anxiety between the values of 4.67 to 1.20.

DISCUSSION

Anxiety in breast cancer survivors is highly prevalent and leads to long-term psychological distress and poor quality of life. Mindfulness based stress reduction is a program focused on self-regulation in relation to fear of recurrence to improve stress and anxiety of cancer patients.[3] In comparison to other types of psychotherapy, the mechanism of MBSR utilizes a variety of professional and self-guided meditative approaches to treat co-occurring symptoms that breast cancer survivors experience after treatment. The unique approach of the MBSR program makes it an effective treatment option for reduction in anxiety for breast cancer survivors.

This review evaluated the efficacy of mindfulness- based stress reduction as an intervention to reduce anxiety of breast cancer survivors. Two out of three studies found improvement in anxiety after intervention with the MBSR program compared to UC. The Lengacher et al. study in 2014 found no difference between the MBSR and UC group. At the start of the study the two groups were not similar, there was no intention-to-treat analysis, and no worst-case analysis. These factors contribute to the study lacking validity. In Lengacher et al. 2021 study, there was a significant difference between the two groups demonstrated by the p-value of 0.01.[7] There was a difference in use of anxiety medications and the MBSR group presented with higher anxiety than the usual care group.[7] This difference introduces bias and decreased validity, since baseline anxiety was not the same amongst all participants. Additionally, there was no allocation concealment, intention-to-treat analysis, or worst-case analysis performed. Lastly, the Hoffman et al. study had a narrow 95% CI of -4.67 to -1.20 and a

mean difference between groups of 2.93, suggesting reduced anxiety in the MBSR group.[6] Although there is a small treatment effect, this study has increased validity compared to the Lengacher et al. 2021. Randomization, allocation concealment and a worst-case analysis was performed.

All three studies had limitations that affected the validity and reliability of the results. In the Lengacher et al. 2014 study patients' symptoms at baseline were low for both groups.[3] Therefore, the effects of MBSR may be minimized due to patients not having significantly severe symptoms of anxiety.[3] Patients were not kept "blind" to treatment in the Lengacher et al. 2014 study and Hoffman et al. study. This bias makes the statistically significant results less valid. Also, in all studies patients completed some degree of self-guided meditative practices, which contributes to potential bias. The three studies assessed only the short-term effects of the MBSR program. Therefore, it cannot be determined if there would be reduction in anxiety for patients long-term.

CONCLUSION

This systemic review had conflicting results between the three studies, and it cannot be determined if MBSR is more effective than standard care in reducing anxiety in breast cancer survivors. Two out of three studies found statistically significant reduction in anxiety but had small treatment effects. MBSR has potential for use in clinical practice, but future studies are warranted to evaluate MBSR before routine use can be recommended for patients. Further studies can be designed to include better measurements of anxiety when selecting participants to strengthen the validity of the results. Also, it is vital to ensure all participants have similar severity and symptoms of anxiety at baseline. Utilizing allocation concealment, intention-to-treat analysis, or worst-case analysis in all studies would help to support the results. It would be

beneficial to determine if MBSR could be delivered at varying program lengths or virtually to make treatment more accessible. There is possibility that future studies will be able to establish a significant use of MBSR in clinical practice.

REFERENCES

1. Vachon E, Krueger E, Champion VL, Haggstrom DA, Cella D, Cohee AA. The impact of fear of cancer recurrence on healthcare utilization among long-term breast cancer survivors recruited through ECOG-ACRIN trials. *Psychooncology*. 2021;30(3):279-286. doi:10.1002/pon.5568

2. De Vries, J., Den Oudsten, B.L., Jacobs, P.M.E.P. *et al.* How breast cancer survivors cope with fear of recurrence: a focus group study. *Support Care Cancer.* 2014;22: 705–712. https://doi.org/10.1007/s00520-013-2025-y

3. Lengacher CA, Shelton MM, Reich RR, et al. Mindfulness based stress reduction (MBSR(BC)) in breast cancer: Evaluating fear of recurrence (FOR) as a mediator of psychological and physical symptoms in a randomized control trial (RCT). *J Behav Med*. 2014;37(2):185-195. doi:10.1007/s10865-012-9473-6.

4. Lebel, S., Tomei, C., Feldstain, A., et al. Does fear of cancer recurrence predict cancer survivors' health care use. *Support Care Cancer*. 2013;21:901–906. doi:10.1007/s00520-012-1685-3.

5. Zheng Z, Yabroff KR, Guy GP Jr, et al. Annual medical expenditure and productivity loss among colorectal, female breast, and prostate cancer survivors in the United States. *J Natl Cancer Inst*. 2015;108(5):382. doi:10.1093/jnci/djv382

6. Hoffman CJ, Esser SJ, Hopkinson JB, Nicholls PG, Harrington JE, Thomas PW. Effectiveness of mindfulness-based stress reduction in mood, breast- and endocrine-related quality of life, and well-being in stage 0 to III breast cancer: A randomized, controlled trial. *J Clin Oncol*. 2012;30(12):1335-1342. doi:10.1200/JCO.2010.34.0331

7. Lengacher CA, Gruss LF, Kip KE, et al. Mindfulness-based stress reduction for breast cancer survivors (MBSR(BC)): Evaluating mediators of psychological and physical outcomes in a large randomized controlled trial. *J Behav Med*. 2021;44(5):591-604. doi:10.1007/s10865-021-00214-0